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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/695,499	10/28/2003	Vincenzo Scarlato	2300-0363.01	7930

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EXAMINER	
GRASER, JENNIFER E	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 03/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/695,499	SCARLATO ET AL.	
	Examiner	Art Unit	
	Jennifer E. Graser	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,3,8,10-13 and 18-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *2 and 3* is/are allowed.

6)☒ Claim(s) *8,10-13 and 18-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/302,626.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Acknowledgment and entry of the Amendment submitted on 9/29/05 is made. Claims 2, 3, 8, 10-13 and 18-21 are currently pending.

Claim Rejections - 35 USC § 112

1. Claims 8, 11, 12, 13 and 19-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 8, 12, 13 and 19-20 recite isolated nucleic acid sequences with a percent identity to a given sequence, but no function is provided for the claimed nucleic acid sequence. It is unclear what function these variants would serve. The claims can be clarified by an amendment, provided there is written support in the specification, stating that the nucleic acid sequence can detect *N.meningitidis* through the high stringency conditions which are to be incorporated in claim 13. Applicants' arguments have been fully and carefully considered but are not deemed persuasive. Their example is not equivalent to the claimed invention because the example is drawn to a full-length protein, not variants with varying homology levels, e.g., as little as 50% homology.

Claim 11 should be amended to recite that the nucleotide sequence is 'fully complementary" to the sequence of claim 8. The term "complementary' can read on as little as one nucleotide.

Claim Rejections - 35 USC § 112-Enablement

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 8, 12, 13 and 18-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for "an isolated nucleic acid sequence comprising SEQ ID NO:3', ' an isolated nucleic acid sequence which encodes a protein comprising the amino acid sequence set forth in SEQ ID NO:4', and isolated nucleic acid molecules which hybridize to these nucleic acid molecule under high stringency conditions (provided they are specifically recited in the claim), does not reasonably provide enablement for isolated nucleic acid sequences which have 50% or greater identity to an isolated nucleic acid sequence set forth in SEQ ID NO:3, isolated nucleic acid sequences which encode 10-mer fragments or isolated nucleic acid sequences which are 80-95% identical to SEQ ID NO:3 with no stated function. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The breadth of the instant claims is drawn to polynucleotides which are not specified in the sequence disclosure. The specification states that substitutions, additions, or deletions may be made to the defined sequences; however, the specification provides no guidance as to what nucleic acids may be changed without causing a detrimental effect to the adhesion and penetration protein to be produced. Further, it is unpredictable as to which amino acids could be removed and which could

be added. While it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where amino acid substitutions can be made with a reasonable expectation of success are limited. Other positions are critical to the protein's structure/function relationship, e.g., such as various positions or regions directly involved in binding, catalysis in providing the correct three-dimensional spatial orientation of binding and catalytic sites. These regions can tolerate only very little or no substitutions. To start with the DNA sequence first, this requires even more work on the part of the skilled artisan.

The instant claims are drawn to nucleic acids comprising a sequence with a given percent similarity to a nucleic acid which encodes a protein. Selective point mutation to one key residue could eliminate the function of the polypeptide. It could eliminate its adhesion and penetration properties. If the range of decreased binding ability after single point mutation of a protein antigen varies, one could expect point mutations in the protein antigen to cause varying degrees of loss of protection/function, depending on the relative importance to the binding interaction of the altered residue. Alternatively, the combined effects of multiple changes in an antigenic determinant could again result in loss of function. A protein having multiple antigenic sites, multiple point mutations, or accumulated point mutations at key residues could create a new antigen that is precipitously or progressively unrecognizable by any of the antibodies in the polyclonal pool. As stated above, Applicants have not shown which nucleotides may be changed without causing a detrimental effect to the protein in which it encodes. The claims allow for as great as 50% variation. This is a huge variation allowing for

many gaps, insertions, substitutions and deletions. It is unclear that a sequence with this much variation would even have the ability to detect *N.meningitidis* in a hybridization assay. Applicants have provided no guidance to enable one of ordinary skill in the art how to determine, without undue experimentation, the effects of different nucleotide substitutions and the nature and extent of the changes that can be made. It is expensive and time consuming to make amino acid substitutions at more than one position, in a particular region of the protein, in view of the many fold possibilities for change in structure and the uncertainty as to what utility will be possessed. See Mikayama et al. (Nov.1993. Proc.Natl.Acad.Sci. USA, vol. 90 : 10056-10060) which teaches that the three-dimensional structure of molecules is important for their biological function and even a single amino acid difference may account for markedly different biological activities. Rudinger et al. (June 1976. Peptide Hormones. Biol.Council. pages 5-7) also teaches that amino acids owe their 'significance' to their inclusion in a pattern which is directly involved in recognition by, and binding to, the receptor and the significance of the particular amino acids and sequences for different amino acids cannot be predicted *a priori*, but must be determined from case to case by painstaking experimental study. The specification also fails to teach the location of immunogenic epitopes. Therefore, it would take undue experimentation for one of skill in the art to determine which 30 nucleotides would encode a 10-mer immunogenic fragment. Given the lack of guidance contained in the specification regarding acceptable nucleotide substitutions, additions or deletions, one of skill in the art could not make or use the broadly claimed invention without undue experimentation.

Response to Applicants' Arguments:

The instant claims are drawn to variants which differ by 50% from the known sequences. This is a very large amount. It is unclear that sequences differing by this much would have the ability to successfully detect N.meningitidis. This is a huge variation allowing for many gaps, insertions, substitutions and deletions. It is even more unlikely that such variants would produce a functional protein or immunogenic fragment. As stated above, Applicants have provided no guidance to enable one of ordinary skill in the art how to determine, without undue experimentation, the effects of different nucleotide substitutions and the nature and extent of the changes that can be made. It is expensive and time consuming to make amino acid substitutions at more than one position, in a particular region of the protein, in view of the many fold possibilities for change in structure and the uncertainty as to what utility will be possessed. Further, it would take undue experimentation for one of skill in the art to determine which 30 nucleotides would encode a 10-mer immunogenic fragment, particularly when no immunogenic epitopes have been identified. Given the lack of guidance contained in the specification regarding acceptable nucleotide substitutions, additions or deletions, one of skill in the art could not make or use the broadly claimed invention without undue experimentation. It is suggested that Applicants limit the claims to molecules displaying greater homology, e.g., 90-95% homology, and which are capable of detecting N.meningitidis through hybridization in order to overcome the rejection.

Claim Rejections - 35 USC § 102- dropped

4. The former rejection of Claims 2, 3, 8, 10-13 and 18-21 under 35 U.S.C. 102(e) as being anticipated by Peak et al (US Patent No. 6,197,312) has been overcome due to Applicants' arguments which have demonstrated their priority filing date is well before the effective filing date of the Peak et al. reference.

Status of Claims:

5. Claims 2 and 3 are allowed.

6. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

7. Correspondence regarding this application should be directed to Group Art Unit 1645. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Remsen. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15,1989). The Group 1645 Fax number is 571-273-8300 which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer E. Graser whose telephone number is (571) 272-0858. The examiner can normally be reached on Monday-Friday from 7:00 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (571) 272-0864.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-0500.

Jennifer Graser
Primary Examiner
Art Unit 1645

2/22/06